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PROTOONCOGENE BCL-2 AND GLEASON SCORE IN PROSTATE CANCER

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Abstract: *The aim of this study was to analyse the relationship between the expression of the bcl-2 proto-oncogene and the histological grading of prostate cancer according to the Gleason score. To study the prognostic significance of Bcl-2 over expression in prostate cancer, 36 consecutive radical prostatectomy specimens were examined by immunohistochemistry. Bcl-2 was associated with malignant phenotype. Bcl-2 over expression (found in 14 – 38.89% tumours) was associated with high Gleason score. These data suggest that altered expression of Bcl-2 plays a role in prostate cancer progression.*

Key words: *bcl-2 protooncogene; Gleason; prognosis; hormone-refractory prostate cancer.*

1. Introduction

The clinical course of prostate cancer is highly variable and cannot satisfactorily be predicted by histological criteria alone. Multiple genetic and epigenetic factors have been implicated in the oncogenesis and progression of prostate cancer. Among the most important regulators of apoptosis and programmed cell death is the bcl-2 gene and its related proteins [8]. Elevated levels of bcl-2 protein may contribute to the progression of prostate cancers to a metastatic and hormone-insensitive state characterized by poor responses to chemotherapy [4].

The aim of this study was to analyse the relationship between the expression of the bcl-2 protoongogene and the histologic grading of prostate cancer according to the Gleason score.

2. Materials and Methods

36 radical prostatectomy specimens of prostate cancer were fixed in 10% buffered formalin and embedded in paraffin wax. Five consecutive sections of 5μm thicknesses were cut from each block and used for haematoxylin & eosin staining for histologic evaluation.

All slides were graded using the Gleason score. According to the Gleason three-grade system tumours were classified as well (Gleason score 2 to 4), moderately (Gleason score 5 to 7), and poorly differentiated (Gleason score 8 to 10).

For the immunohistochemical staining an antibody to bcl-2 protein (DAKO clone 124) was used according to the avidin-biotin-complex method.

Imunohistochemical evaluation was performed under a light microscope at 10x magnification. In each case, the whole tumour surface was analyzed, noting the presence or absence of staining. The resulting bcl-2 staining data were evaluated for association with histological features (Gleason score). Statistical analysis was performed by Statistics for

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Windows (StatSoft Inc) program. Comparison between means was performed using the Student's *t*-test; $p<0.05$ was considered significant.

3. Results

In 36 cases of prostate cancer, Bcl-2 expression was positive in 14 (38.89%) (Table 1) and was typically found in the cytoplasm of prostate cancer cells, predominantly of the basal layer (Figure 1). As shown in Figure 2, increased Bcl-2 expression was associated with higher Gleason score, without any significant correlation. Bcl-2 expression was significantly higher in low differentiated samples than in well differentiated prostate cancer samples ($p=0.01$).

Bcl-2 positive tumors vs Gleason score Table 1

Gleason score	No. (%) of bcl-2 positive tumours	No. (%) of bcl-2 negative tumours
2-4	1 (8.33%)	11 (91.67%)
5-7	5 (41.67%)	7 (58.33%)
8-10	8 (66.67%)	4 (33.33%)
Total	**14 (38.89%)**	**22 (61.11%)**

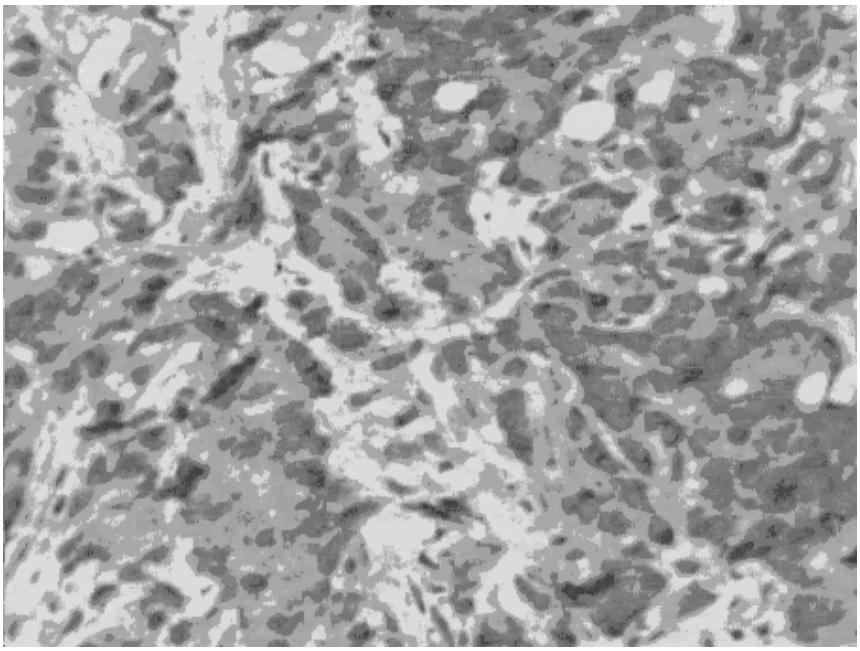

Fig. 1. *Cytoplasmic staining in a low differentiated prostate carcinoma (Gleason 4+5), 20x (Bcl-2).*

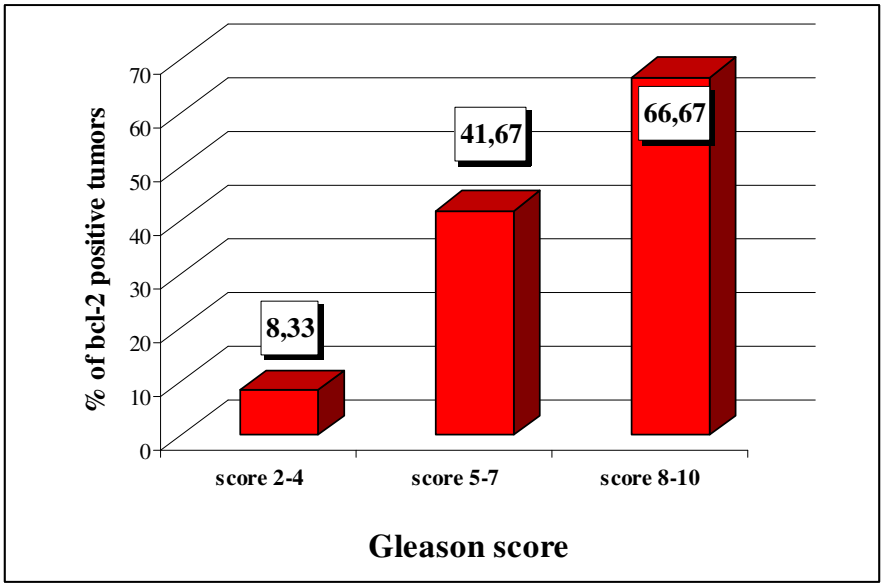

Fig. 2. *Frequency of bcl-2 positive tumours vs histologic grading (Gleason score)*

4. Discussion

Antiapoptotic Bcl-2 molecules are believed to regulate the sensitivity of cells toward either survival or apoptosis [6].

Over expression of Bcl-2 is frequently associated with poor prognosis in several cancers, including prostate cancer [1, 2, 7].

In this study, Bcl-2 expression was correlated with a higher Gleason score. This positive association of Bcl-2 expression with worse clinico-pathologic characteristics is consistent with previous reports [1, 2, 3, 5, 9]. These findings suggest that up-regulation of antiapoptotic Bcl-2 protein may interact with the processes involved in the development of hormone-refractory prostate cancer as well as disease progression in prostate cancer.

6. Conclusions

Bcl-2 over expression is associated with aggressive biological features of individual prostate cancers and appears to be associated with the development of hormone-refractory prostate cancer.

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